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THE USE OF PITUITARY EXTRACT IN OBSTETRICS.

Thesis for the degree of M.D. 1914.

by

Robert Marshall Allan, M.B., Ch.B.

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1914.



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## THE USE OF PITUITARY EXTRACT IN OBSTETRICS.

### INTRODUCTION.

From the earliest times the pituitary body has been regarded as possessing a secretory function. Galen and Vesalius believed that the mucus (pituita) formed in the brain was excreted by the pituitary body. Vieussens, Sylvius, Willis and others considered that the cerebrospinal fluid was secreted by it. Practically no further attention was paid to the gland until Marie in 1886 described the clinical condition called acromegaly and showed that it was invariably associated with tumours of the hypophysis. The first important advance in our knowledge of the gland was made by Oliver and Schäfer (1) in 1895, and their results are referred to later. In Obstetrics no advantage was taken of these discoveries until Blair Bell (2) published a paper in 1909. Since then a considerable literature has arisen. It is mainly German in origin and few English papers have yet appeared.

The work on which this thesis is based was conducted at the Rotunda Hospital during my term of office there as Assistant Master.

For the sake of clearness the thesis has been divided into two parts - the first comprising a brief outline of the main facts regarding the gland; the second giving the results obtained and the conclusions to which I have come.

## ANATOMY AND HISTOLOGY OF THE GLAND.

The pituitary gland is situated within the cranium, at the base of the brain, in a depression of the sphenoid known as the sella turcica. It is connected to the brain by a stalk or infundibulum. The sella turcica is lined with dura mater, which forms a covering over the gland - the diaphragma sellae turcicae. The lateral boundaries are formed by the cavernous sinuses and the gland lies in the anterior angle of the optic commissure.

It consists of two lobes - anterior and posterior.

The anterior lobe is hard, kidney shaped and concave posteriorly, and pale yellow to greyish red in colour.

The posterior lobe is smaller, more rounded, white and soft. It fits into the concavity of the anterior lobe.

There are three types of mammalian pituitary body, viz:-

- A. That in which the posterior lobe is hollow and the cavity is in free communication with the Third Ventricle. The epithelium of the anterior lobe almost completely surrounds the posterior lobe, e.g., the cat.
- B. That in which the body of the posterior lobe is solid/

solid but the neck is hollow, and communicates with the Third Ventricle. The posterior lobe is surrounded by the epithelium of the anterior lobe, e.g., the dog.

- C. That in which the body and neck of the posterior lobe are solid, though there are traces of a cavity in the neck. The epithelium of the anterior lobe does not spread so far round the posterior lobe, but is gathered around the neck and spreads over and into the adjacent surface of the brain, e.g., man, the monkey, ox, pig and rabbit.

The anterior lobe or epithelial portion is again divided into two parts - an anterior lobe proper and an intermediate portion. Between the two is a cleft-like space containing glairy fluid.

The pituitary gland therefore consists of three parts:-

- (1) Anterior lobe.
- (2) Pars intermedia.
- (3) Posterior lobe.

#### (1) Anterior Lobe.

This consists of solid columns of cells between which are thin walled blood sinuses. The cells are frequently placed directly on the delicate endothelium of the vessel walls. These cells consist of two types:-

- A. Chromophil - composed of eosinophils and basophils with numerous granules and having the characteristic/



characteristic appearance of a gland of internal secretion.

B. Chromophobe - comprising neutrophils.

These are the principal cells (Hauptzellen of the Germans). Colloid material is also present.

### (2) Pars Intermedia.

Consists of finely granular neutrophil cells arranged in layers of varying thickness closely applied to the body and neck of the posterior lobe and to the under surface of adjacent parts of the brain.

The part separated from the anterior lobe by the cleft has practically no blood vessels. Colloid material occurs between the cells and passes through the posterior lobe to the Third Ventricle.

### (3) Posterior Lobe.

This consists of neuroglial cells and fibres and is invaded by the epithelial cells of the pars intermedia. The glial cells are long and cylindrical with granular protoplasm and several nuclei. Colloid is also present and is a secretory product of the epithelial covering of the pars intermedia. Cushing and Goetsch (3). The neuroglial threads also contain a greenish yellow pigment supposed to be a product of metabolism. Herring (4), Cushing (5), Biedl (6).

During pregnancy there is a remarkable increase in size, weight and appearance of the gland. The change occurs chiefly in the anterior lobe, which becomes/

becomes softer and when squeezed exudes a milky fluid. Pregnancy cells, derived from the principal cells, make their appearance. They outnumber the eosinophils, while the basophils remain unaltered. They have a granular protoplasm staining with eosin and large irregular nuclei. They form agglomerations suggesting an adenomatous hyperplasia. After parturition they involute and reassume their former appearance of principal cells. In subsequent pregnancies they are increased in amount. Erdheim and Stumme (7).

#### DEVELOPMENT.

The gland makes its appearance early in embryonic life. In mammals the epithelial portion is derived entirely from Rathke's pouch - an invagination of the buccal ectoderm. It is soon distinguishable into two parts. One of these, the pars intermedia, is closely adherent to the wall of the cerebral vesicle; the cells are clear and tend to form colloid. The other portion of the buccal epithelium gives rise to the anterior lobe proper, and forms solid columns of granular cells separated by blood channels. The posterior lobe is an invagination of the part of the thalamencephalon, which is adherent to the anterior and upper wall of Rathke's pouch. It therefore possesses an epithelial covering derived from the latter. The infundibular process grows backwards and in the cat retains its central/



central cavity. It is lined by ependyma cells, which become elongated. The posterior lobe is from the first a composite structure of epithelium of the pars intermedia and of neuroglia and ependyma.

To summarise - the anterior lobe and pars intermedia are derived from an upgrowth of the buccal cavity; the posterior lobe from a downgrowth from the Third Ventricle. Herring (4).

#### PHYSIOLOGICAL ACTION OF PITUITARY EXTRACT.

The characteristic action of extracts of the pituitary body is stimulation of plain muscle fibres. Different organs containing these fibres show a varying sensitiveness of response to the extract, the arteries, uterus and spleen being mainly affected. Oliver and Schäfer (1) found that aqueous or saline extracts of the whole gland produced a rise of blood pressure due to vaso-constriction of the peripheral arterioles. It is more prolonged but not so intense as the action of adrenalin. The difference between the two, however, is that pituitary extract has a direct action on the muscle, while adrenalin affects the peripheral nerve terminals. (Dale (8).

Howell (9) then proved that extracts of the anterior lobe are devoid of physiological activity; whilst those from the posterior lobe produced the results/

results obtained by Oliver and Schäfer. There is a rise of blood pressure accompanied by slowing of the heart. The latter phenomenon is not constant and when present is not abolished by section of the vagi or the action of atropine. It is therefore peripheral in origin. Schäfer and Vincent (10).

After the injection of a second or third dose there is no rise of blood pressure but invariably a fall, which is of short duration. This is due to a second substance present in the extract - a depressor. It is soluble in alcohol, while the pressor substance is insoluble. It is not choline as stated by several observers.

But besides these two constituents of an extract of the posterior lobe, there is another substance which acts specifically on the renal vessels, producing dilatation and diuresis. This substance is soluble in water and is not destroyed by boiling. Schäfer and Herring (11).

Bell (2) and Dale (8) were the first to experiment with the extract on the uterus. It causes powerful contractions, which occur whether the animal be pregnant or not. A second injection causes a relatively more marked contraction unaccompanied by rise of blood pressure. I have confirmed this point also clinically. Frankl Hochwart and Fröhlich (12) have shown that in dogs and rabbits it induces contractions/

contractions of the bladder and raises the faradic irritability of the vesical autonomic fibres, while the irritability of the vesical sympathetic fibres remains unaltered. Similarly the uterus of the rabbit during pregnancy or lactation undergoes a long continuous contraction with an increase in irritability of the uterine sympathetic nerves. It has no action on any other organs innervated by the sympathetic system.

Schäfer and Mackenzie (13) state that the extract is a powerful galactagogue. But Heaney (14) has almost conclusively proved that any action it may possess is on the unstriated muscle of the breast and not on the milk ducts. It causes contractions of the breast but does not directly stimulate the secretory mechanism of the glands.

While the anterior lobe does not cause any of these effects, its administration produces an increase in growth of the bony and connective tissue. Starling (15).

The part of the gland producing the active principle.

Howell (9) showed that the posterior lobe alone contained the active principle. But this lobe is composed of a mixture of nervous and epithelial elements, the latter from the pars intermedia. Osborne and Vincent (16) found that extracts of the central part of the posterior lobe (without any epithelial elements) gave all the above mentioned results.

However Schäfer (17) and Bell (2) maintain that the/



the epithelial cells of the pars intermedia and the posterior lobe together form the colloid material containing the active pressor principle. And all the commercial preparations of the gland are made from both these parts.

#### Chemistry of the Active Principle.

It is unaffected by boiling and is soluble in water and saline solution. Schäfer and Vincent (10) show that while the pressor substance is soluble in water, it is insoluble in alcohol and ether. The depressor substance is soluble in both alcohol and ether. The exact composition is as yet unknown. It is not a protein as it withstands boiling; it is not adrenalin, as it has different reactions; nor is it thyroïdin as it contains no iodine. Cushing (5).

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For the sake of clearness, my results have been classified under the following heads:-

1. Preparation used, dosage, methods of administration, etc.
  2. Effect on the uterus.
  3. Effect on the foetus.
  4. Indications  
    before labour  
    during labour  
    after labour.
  5. Contraindications.
  6. Use in placenta praevia.
  7. After results.
  8. Conclusions.
  9. Tables and Diagrams.
  10. Bibliography.
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PREPARATIONS USED.

The commercial preparations are:-

Infundin (Burroughs and Wellcome),

Pituitrin (Parke Davis ), and

Pituglandol (Hoffmann La Roche).

I have had experience only of Infundin. Those who have tried all three state that there is no difference in action between them.

DOSAGE.

1 c.c., = 0.2 grms. of the extract, and this strength was used in all the cases. Edgar (18) recommends double this dose. But I have never found it necessary and there is always the possibility of inducing too powerful contractions with consequent danger of cervical laceration or uterine rupture, especially if the cervix be not fully dilated at the time of administration.

METHODS OF ADMINISTRATION.

The extract is given hypodermically. The syringe should always be sterilized by boiling in plain water. It should not be stored in alcohol because even traces of this will destroy the extract.

Injectons may be given subcutaneously, intramuscularly or intravenously. I had always given intramuscular/



intramuscular injections until the publication of a paper by Heaney (14). He says "Because of the possibility of an undiagnosed condition contraindicating an upright increase in blood pressure and arteriole contraction, the intravenous administration is unsuited for routine use, and should be reserved for emergency cases where immediate action is highly desirable, such as severe post partum haemorrhage. Where a fairly rapid result is wanted intramuscular administration is much safer. For general use subcutaneous injection should be employed, since it is without possibilities of harmful blood pressure effects and is as safe as far as the skin is concerned as the ordinary hypodermic medication".

Since reading this I substituted subcutaneous for intramuscular injections with better results. The duration of the action of the drug was prolonged and the contractions of the uterus were more regular. It acted as a gentle stimulus more than a sudden one, which usually occurred with intramuscular injections. It may be injected into any part of the body, usually the arm or the thigh.

The drug is not poisonous to the mother even in big doses and is not cumulative in its effect if repeated doses are given. But there is one important point, viz., that the drug apparently tends to deteriorate if kept too long. Turenne (19).

In/

In several cases I could only ascribe failure to this cause. Failures may also be possibly explained in the light of an observation by Kleeman (20). He found that an extract made from pregnant animals had an unstable action; it was both vaso-constrictor and dilator. Whereas extracts from animals which had not recently been pregnant gave the usual results.

In my series there were five cases of absolute failure - the drug producing no effect on the uterine contractions.

#### EFFECTS ON THE UTERUS.

Blair Bell (2) states that "pituitary extract causes powerful contractions of the pregnant, puerperal and menstruating uterus". My own observations were made by placing the hand over the contracting uterus and timing each pain and the interval between them. The contractions still retain their physiological character. With very few exceptions they are rhythmical and intermittent but not tonic (see diagrams). This fact must be strongly emphasised for it is the basic principle governing the use of the extract in obstetrics. The exceptions were a few cases in which the final pain seemed to extend over an interval of several minutes (see diagrams 7 and 8). But even in these the contractions were not what might properly be called tonic, as regular slight relaxations were always/

always observed during the pains. These pseudo tonic contractions invariably occurred when the presenting part was about to be delivered. Therefore one is justified in regarding them as a simple exaggeration of the normal characteristic of the pain at that time, when they are practically continuous. These exceptions probably correspond to the "Sturmwehen" recorded by several German observers. I have never seen genuine tonic contractions occur.

When the extract was administered during the second stage, the interval elapsing from the time of injection to the onset of the first pain varied from two to six minutes, with an average of three and a half minutes. Pains occurred at an average interval of one and a half minutes, whereas normally one would expect an interval of two to four minutes. The birth of the child followed on an average of seventeen minutes after the injection. If it did not take place the effect of the drug lasted forty to fifty minutes.

The placenta was always spontaneously expelled, except in four cases where it was adherent and required manual removal. In no case was there any suspicion of incarceration - a danger referred to by some observers.

Strassmann (21) noticed an earlier detachment and expulsion of the placenta. This coincided with my own/



own results. For the placenta was ready for expression in eighteen minutes in primiparae and in eleven minutes in multiparae. In nine cases (two primiparae and seven multiparae) it was expelled immediately without any ill effects. These results differ somewhat from those of the Wertheim Klinik (22). From an experience of 400 cases they were of the opinion that the duration of the third stage was frequently lengthened and only seldom shortened.

Although Fischer (23) and most other observers state that the effect of the injection is better the further advanced in labour the patient is at the time, this does not prevent its use during the first stage. Twenty patients (six primiparae and fourteen multiparae) were given injections during the first stage for primary inertia. It was administered in primiparae when the cervix was three quarters dilated and was followed by the birth of the child in two hours; in multiparae the cervix was about one quarter dilated and birth followed in an average of forty minutes. In several multiparae the action was extremely rapid, birth occurring in five to ten minutes with no ill effects (see diagrams 1 and 2). But it must be emphatically stated that in none of these cases was there a suspicion of any obstruction whatever to the birth of the child. For its administration is unjustifiable and dangerous under these circumstances.

An/

An anaesthetic does not interfere with the action of the drug. Recently several observers have used it in combination with morphia and scopolamine. I have used it with morphia in a small number of cases and have been very satisfied with the results. The morphia quietens the patient and deadens the pain of the increased contractions caused by the extract. Even if the foetus be not expelled spontaneously, the effect on dilation of the cervix or vagina is so marked that the application of forceps is rendered in many cases easy. There were nine cases in which the forceps had to be applied because the extract did not produce birth of the child.

These observations are concerned with the uterus at full term. But when given to cases early in pregnancy the results are not so certain. This matter is more fully dealt with under the indication for its use. Watson (24) states that when given late in the first or second stages at the term the polarity of the contractions is not interfered with, but in abortions and early in the first stage one is very liable to get spasm of the cervix. This complication has also been observed by Ham (25) and Reick (26). I have never seen it.

#### EFFECT ON THE FOETUS.

Hoffbauer (27) and Fischer (23) noted a slowing of/  
of/

of the foetal heart after injection. But both are emphatic that there is no permanent ill effects on the child. I found it not unusual for the foetal heart to temporarily drop to 120 or even 100, but except in a few cases the child was born in good condition (see diagrams 6 and 7). The exact cause of this alteration is not known. The most obvious explanation is that as the pains follow one another at short intervals, the foetal blood does not get time to be sufficiently oxygenated. Recently Hecht and Nadel (28) have advanced a theory which is very alluring and may explain these cases. From their experiments on animals they came to the conclusion that the extract has a stimulating action on the vagus and also on the secondary centres in the heart, especially the bundle of Tawara and on the apex of the left ventricle. The consequent bradycardia was prevented by the use of atropin. This contradicts the observations of Schäfer and Vincent quoted previously. Therefore they advise the use of atropin in all such cases and state that it has no effect on the action of the pituitary extract on the uterus.

The exceptional cases referred to above numbered ten. One occurred in a multipara, the child being born in white asphyxia and not recovering; but it should be stated that it was a premature twin of 35 weeks. The other nine occurred in primiparae. Five were/



were dead born and four were born in white asphyxia, two recovering. This still leaves a foetal mortality of seven. Two of these had the cord tight round the neck and one was a difficult breech delivery in a case of contracted pelvis with a conjugata vera of 9 cms. It is hardly fair to attribute the loss of these three children to the use of the extract; so if they be excluded, there still remain four deaths unaccounted for except as a possible result of the injection.

As this effect on the foetus is of the greatest importance the histories of these cases are given in detail.

In one the foetal heart was heard at a certain time to be 140, eight minutes later it had dropped to 100, forceps were applied at once but too late. The patient was a primipara and there was probably a minor degree of contracted pelvis present, as the head was unfixed for some time after labour had commenced.

In the second case a similar sudden drop was observed. The foetal heart was 128 five minutes before delivery and the child born spontaneously was dead. The third case was one of contracted pelvis with a conjugata vera of 9.25 cms. The pains became weak when the cervix was fully dilated and the head through the brim. Strong contractions followed the injection for thirty minutes and then became weaker. The injection was repeated and the child expelled in half an/

an hour. During this time there were no signs of foetal distress and nothing unusual was noted about the foetal heart.

There was more gradual slowing in the fourth case and forceps were applied as soon as possible but too late to save the child.

A comparison of the foetal mortality between cases treated with pituitary extract and those treated with forceps alone is interesting. From June 1912 to June 1914, 180 cases were treated by pituitary extract, in the vast majority of which forceps would have been applied and only four foetal deaths could not reasonably be accounted for. During the same period 122 cases were treated by forceps alone with a foetal mortality of 19. These figures help to prove that there is at least no additional risk to the foetus attending the use of the drug. And if the absence of intrauterine manipulation and consequent decrease in the maternal morbidity be taken into account, one would advocate its use in most cases where forceps seem the only alternative.

### INDICATIONS.

#### Before labour.

- (a) Pituitary extract has been used as a means of emptying the uterus in cases of abortion. Stern (29) and Fischer (23) report two cases each of whom/

whom were failures. I have also been unsuccessful and as far as can be learnt from a careful study of the literature, the drug is little better than useless so early in pregnancy.

- (b) It has also been administered for the purpose of inducing premature labour and in this respect the results were more encouraging.

Stern (30) reports three successful cases for pulmonary and laryngeal tuberculosis - two with pituitary extract and one in combination with the Champetier de Ribes' bag.

Pouliot (31) reported six cases - three for minor degrees of contracted pelvis with two successes; three for cases of premature rupture of the membranes - all successful. But he states that the drug may have only augmented contractions which were bound to come.

Hirsch (32) reports four cases, all successful.

Lindemann (33) induced labour at term in four cases, with one failure. My own experience is limited to one case of chronic nephritis, seven months pregnant. The injection was repeated and the birth of the foetus followed in six hours.

In spite of these successes there scarcely seems sufficient evidence yet to allow any definite conclusions to be drawn regarding its value in inducing labour unaided. Benthin (34) maintains that the extract alone has no effect on the uterus when not in labour, since/



since it is refractory at this time and does not respond; whereas it does respond to the smallest dose when in labour.

- (c) But when used as an adjunct to induction of labour by version or the Champetier de Ribes' bag its use is distinctly valuable. I have given it in two such instances; the first was in a case of dead foetus after version when pains had not come on for three hours. Strong contractions followed the injection of 1 c.c. and birth of the foetus resulted in five minutes.

The other case, though not exactly one of induction of labour, yet illustrates the value of the combined treatment. It was one of transverse presentation with the cervix one quarter dilated, an arm prolapsed and no pains. After internal cephalic version a tight binder was applied and 2 c.c.s produced birth of a living child in 45 minutes.

#### During Labour.

This is universally regarded as the best time for its administration.

- (a) Its chief indication then is secondary uterine inertia especially when the cervix is fully dilated and the head well through the brim. By its use at this time the application of forceps can in the majority of cases be avoided.

143 patients (105 primiparae and 38 multiparae) received/

received the drug for inertia in the second stage. The average duration of labour before injection was nineteen hours in primiparae and seven hours in multiparae. The time elapsing between the injection and birth of the child averaged twenty two minutes and eleven minutes respectively.

(b) Twenty patients (6 primiparae and 14 multiparae) received injections for primary inertia. The duration of labour before administration of the drug was twenty hours in the primiparae and thirteen hours in the multiparae. The time after injection until the birth of the child was on an average two hours, and forty minutes respectively.

(c) Excellent results were also obtained in nine cases of over-distension, i.e. hydramnios and twins, where the uterus had become inert after rupture of the membranes. As these are really cases of inertia they have been included in the above.

(d) The question of its use in minor degrees of contracted pelvis is of considerable importance. Despite the strong support given to this indication by most authorities, my experience has not been so fortunate. It was administered in three cases with fatal results to the child in each. These cases have been referred to already. In one the extract may be exonerated from blame, as it was a difficult/

difficult breech delivery through a pelvis with a conjugata vera of 9 cms.; but there was no extenuating circumstances in the other two. Apparently the cause of the trouble is that the foetus has been already sufficiently compressed by the efforts of the uterus to drive the head through the brim. It is therefore unable to withstand the extra pressure resulting from the increased pains produced by the drug. Another factor, which probably plays an important part, is that at this time the head has just reached the pelvic floor and this is in primiparae resistant. So that the foetus is compressed between the uterus and the perineum and is unable to withstand the pressure.

From my experience of these cases I would certainly hesitate to give the drug if there was any disproportion between the presenting part and the pelvis.

- (e) The extract may also be given as a prophylactic to multiparae with a history of post partum haemorrhage or retained placenta in previous labours. The correct time for such an injection is just prior to the birth of the child. It was so given in two cases, both successful.
- (f) Prior to performing Caesarean Section the extract may be injected. The uterus contracts well but I have never seen it become the "small blanched ball"/



ball" described by several authors. I could not satisfy myself that it possessed any marked advantage over ergot. As Edgar (18) states, it has a quicker action but otherwise is not superior to the older remedy. For reasons given in the next section it was usually employed by me in combination with some preparation of ergot.

#### After Labour.

- (a) Post partum haemorrhage was the original reason for its employment in Obstetrics, Bell (2). While it was given alone by the earlier investigators, the majority now use it in combination with a preparation of ergot. Although it only intermittently contracts the uterus, it raises the blood pressure and counteracts shock. The ergot does the major part in controlling the haemorrhage by inducing tonic contractions of the uterus. We have used it as a routine at the Rotunda Hospital for all cases and the results were good. I have had no experience of the intravenous method of administration in severe cases. Kreiss and Kehrer (35) state that 0.5 - 1 c.c. should be given in half a minute. If more quickly injected there is a liability to collapse, pallor and shallow rapid breathing with a small thready pulse. The first effect is an immediate rise in the blood pressure and temporary cessation of respiration. This is followed/

followed by a fall in blood pressure and then a rise and uterine contractions become regular.

Undoubtedly in pituitary extract we have a very powerful remedy to combat post partum haemorrhage, and it has taken a recognised place in the treatment of this serious condition.

- (b) Vogt (36) recommends that it should be used in all cases of retained placenta before attempting manual removal. I have not tried this with any case.

#### CONTRAINDICATIONS.

- (a) Patients suffering from chronic renal disease, with raised blood pressure, and chronic cardiac disease have been considered as unfavourable subjects for its use.

Trapl (37), however, from an experience of 177 cases states that carditis and nephritis are not definite contraindications, although he advises cautious employment of the drug.

Stern (38) has induced labour with repeated injections in cases of nephritis without any ill effects. I have successfully induced labour in a severe case of chronic nephritis without the slightest injury to the patient and have also used it in several cases of simple albuminuria with no bad effects.

- (b)/

- (b) Eclampsia is practically unanimously regarded as a contraindication because of the condition of the blood pressure. Still Schlossberger (39) reports two cases in which the extract was given and it apparently cured the fits.
- (c) Cardiac disease, whether compensated or not, should be regarded as a contraindication. My experience is limited to one case. The extract was given to a patient who was admitted in labour and suffering from bronchitis. Heart trouble was not suspected, and no physical examination had been made. Twenty minutes after the injection she suddenly collapsed with cyanosis, dyspnoea and a rapid pulse. Forceps were at once applied and she recovered after stimulants had been given. Then a mitral lesion was discovered.
- (d) It should never be employed if the symptoms of threatened rupture of the uterus are present.
- (e) Marked disproportion between the foetus and the pelvic passages, or any malpresentation are also contraindications.
- (f) One would hesitate to use it in cases where the uterus had been weakened by scars from operations as Caesarean Section or myomectomy.
- (g) When the foetus shows signs of distress it is better not to give it, unless one is prepared for rapid delivery should the occasion arise.



USE IN PLACENTA PRAEVIA.

Most promising results have been recorded regarding its use in this condition.

Very few cases can be traced where it has been used unaided. Hoffbauer (40) is a strong advocate of its employment in cases of lateral placenta praevia, the only other treatment being rupture of the membranes. As an adjunct to treatment by version or the Champetier de Ribes' bag, its use is almost imperative if one expects to save the child; while the advantage to the mother is apparent owing to the rapidity with which birth follows version. Trapl (41) reports sixteen cases (fifteen lateral and one central) with only three foetal deaths. Gall (42) had ten cases (nine central and one lateral) with three foetal deaths. But in all of these no foetal heart was heard and the extract was given for maternal reasons. I have had seven cases (four lateral and two marginal and one central) with two dead children. While these cases are not numerous the foetal mortality was only 28% - a very encouraging result when we consider that at present the average mortality stands at something between 40-60%. The only objections which can be raised against its use are that frequently the mother requires a period of rest after version has been performed in order to recover from the shock caused by the haemorrhage. Also that as the foetus is frequently premature/

premature its chances of living are not great and owing to the condition of the cervix in placenta praevia there is a great risk of severe laceration by rapid delivery. These objections are outweighed by the shortening of the period of labour and consequent greater chance for the child and subsequent/<sup>good</sup> contractions of the uterus. The cervix was never lacerated in any of my cases; nor has any such case been yet recorded.

#### AFTER RESULTS.

(a) Postpartum atony of the uterus with slight haemorrhage has been observed by many. Oppenheimer (22) states that 7% of his cases had it. This atony is most liable to occur when more than one hour elapses between injection of the extract and birth of the child, because of the relaxation of the uterus which occurs after the effect of the drug has worn off. Six of my cases showed this, but in only one was there more than an hour between injection and delivery. She was a multipara with a history of post partum haemorrhage in previous labours. In each case the uterus hardened after massage and ergot, so they are not true cases of post partum haemorrhage.

(b) Schmidt (43) observed after pains in 50% of his cases. No other authority has reported such an occurrence/

occurrence and I have never seen it.

- (c) There were five morbid cases (B.M.A. standard), four of which were associated with forceps. This reduces the morbidity to one out of all the patients treated with the extract alone. If we consider that the average morbidity with forcep operations is 20%, and that the majority of these cases would otherwise have been so delivered, the result as far as maternal morbidity is concerned is highly satisfactory.
- (d) Although only three babies required artificial feeding I could not satisfy myself that the extract had a specific effect in promoting the milk supply.
- (e) My results regarding the results on intestinal peristalsis and on the bladder were also frankly negative. Edgar (18) had a similar experience.

#### CONCLUSIONS.

1. Pituitary extract is uncertain in its action during the earlier months of pregnancy, unless when used in combination with other methods. The nearer to term the patient is, the surer the effect of the drug.
2. It undoubtedly increases the strength of the uterine contractions.
3. These strengthened contractions maintain their physiological/



physiological character and are never tonic.

4. The best results are obtained when given for uterine inertia, especially the secondary variety.
5. It reduces the number of forceps operations with a consequent lessening of morbidity.
6. The puerperium is normal.
7. It gives improved results both for mother and child in cases of placenta praevia if used in combination with version.
8. When given with ergot it is extremely valuable in the treatment of post partum haemorrhage.
9. It is as suitable for the private as for the hospital patient. Its administration involves no extra trouble nor anxiety beyond the fact that the foetal heart must be carefully and repeatedly noticed after its injection.

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The main results I have obtained are summarised in the following tables:-

Table A.

Indications	No. of cases	Para		Method of Delivery		Result to child	
		Primi- parae	Multi- parae	Spontaneous	Forceps	Alive	Dead
Primary Inertia	20	6	14	16	4	17	3 *
Secondary Inertia	143	105	38	138	5	138	5 *
Placenta Praevia	7	2	5	7	-	5	2
Prophylaxis in cases of previous post partum haemorrhage	2	-	2	-	-	-	-
Induction of Labour							
Alone	1	-	1	1	-	-	1 macerated
Combined with other methods	2	-	2	2	-	1	1 macerated

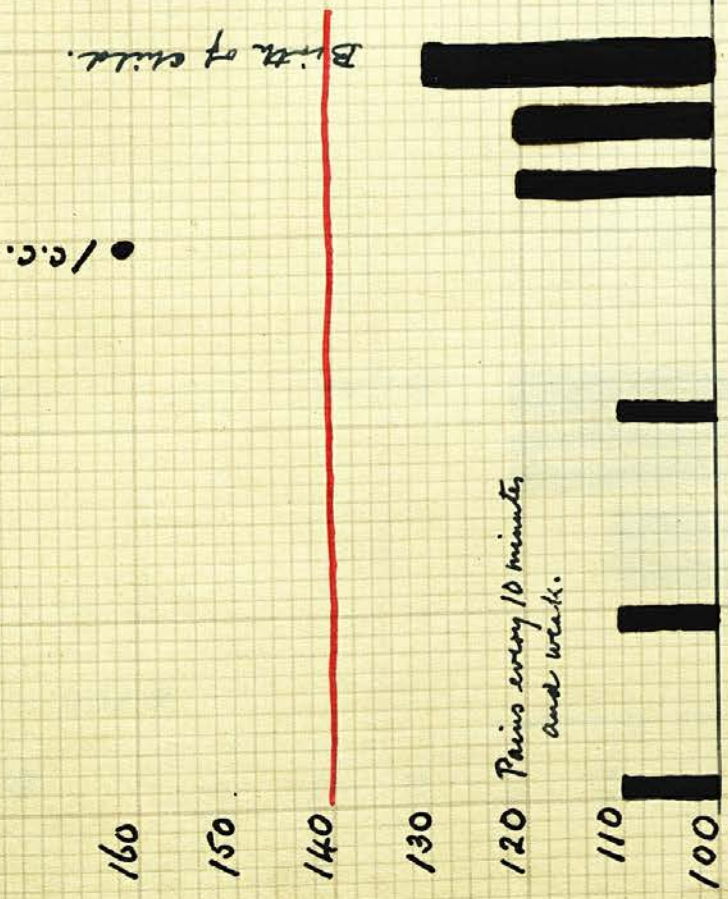
\* Three patients with dead children had contracted pelves.

Table B.

Indications	No. of Injections.			Average duration of labour before injection.		Average interval to onset of pains.	Average interval to birth of child		Average length Third Stage.	
	One	Two	Three	Primi-parae	Multi-parae		Primi-parae	Multi-parae	Primi-parae	Multi-parae
Primary Inertia	15	4	1	<u>hours</u> 20	<u>hours</u> 13	<u>minutes</u> $3\frac{1}{2}$	<u>hours</u> 2	<u>mins.</u> 40	<u>mins.</u> 20	<u>mins.</u> 18
Secondary Inertia	131	9	2	19	7	$3\frac{1}{2}$	<u>mins.</u> 22	11	18	11



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Each vertical space represents 1 minute  
 The thick vertical columns represent the pains, their duration and intensity.  
 A column from 100 to 110 represents a weak pain.  
 " " 100 to 120 " " medium " "  
 " " 100 to 130 " " strong " "  
 Fœtal heart.

C.C. age 37. XI para.  
 Os fully dilated, membranes ruptured and head past the brim when extract injected.

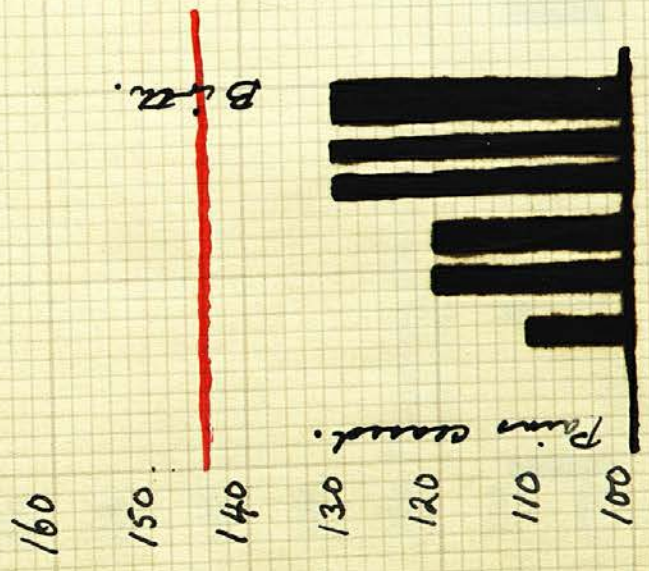
Indication - Secondary inertia  
 F.H. unaffected.

Placenta in 5 minutes.  
 Relaxation of uterus  $1\frac{3}{4}$  hours later but no P.P.H.



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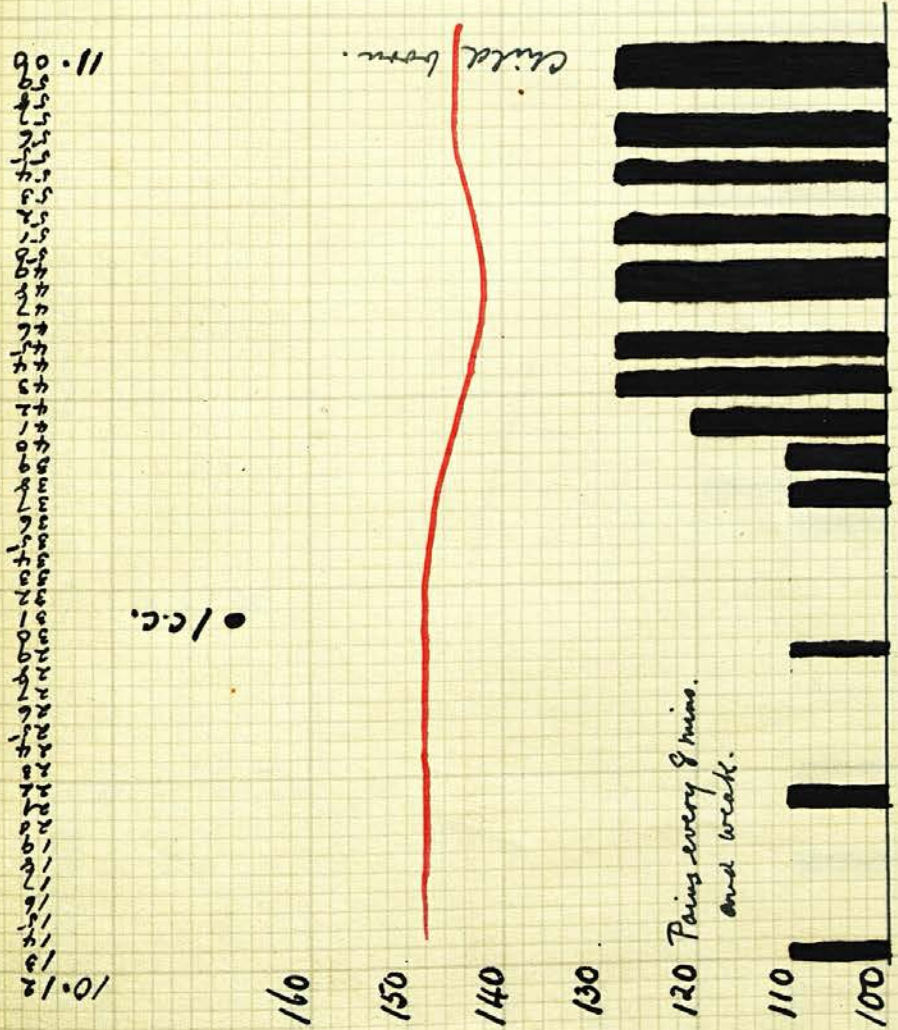
• 100.



See Diagram I for explanation of scheme.

C. McCA. aged 22 II para. So fully dilated, membranes ruptured 9 hours, head well down in pelvis. Pains had ceased.  
Indication - Secondary Inertia.  
F. H. unaffected.  
Placenta in 15 minutes  
hs P. P. H.





See Diagram I for explanation of scheme.

G.S. age 25 I para.  
 Os fully dilated, membranes ruptured, head on perineum for 2 hours.  
 Indication - Secondary inertia.  
 F.H. practically unaffected.  
 Placenta in 20 minutes.  
 No P.R.H.







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• / c.c.

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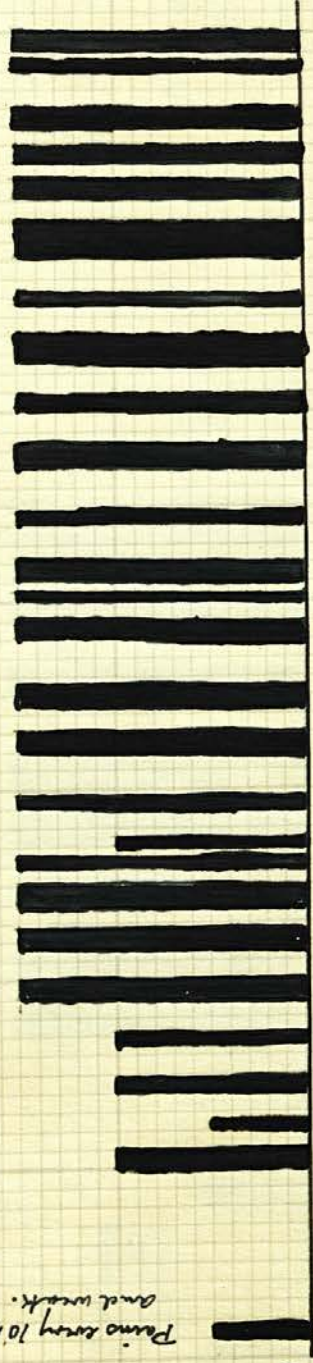
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B. i. t. a.

Pain every 10 mins  
and week.

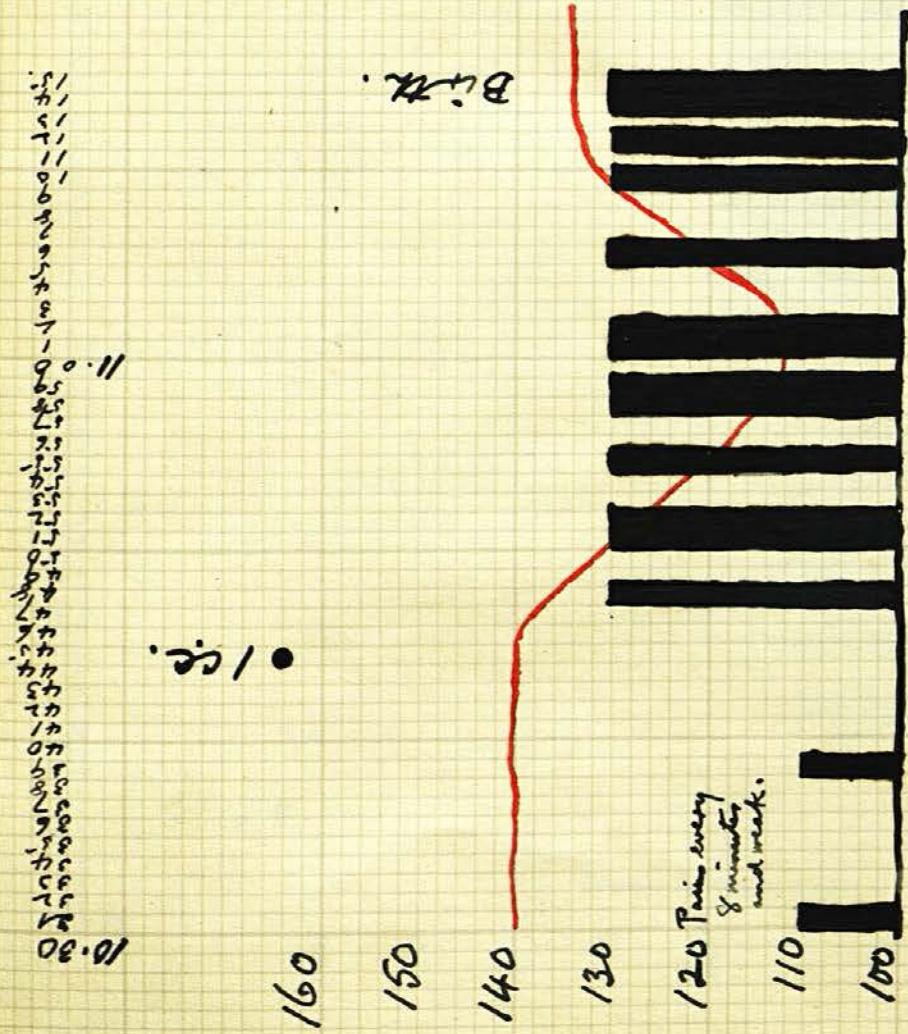


A. H. age 23 I para.  
As fully dilated,  
membranes ruptured,  
head well down but  
not on perineum.  
Induction - Secondary  
inertia.

See Diagram I for explanation of scheme.

F. H. unaffected  
Placenta in 10 minutes  
to P. P. H.





T. R. aged 38 I para.

Os fully dilated, head on perineum, membranes ruptured. In second stage 6 hours. Pains weak and infrequent.

Indication - Secondary Inertia  
F.H. shows marked drop  
and then recovery.  
Placenta in 10 minutes.  
no P.P.H.



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• / c. c.

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Pain practically ceased.

Birth.



See Diagram I for explanation of scheme.

S.D. age 23. II para.

As fully dilated, membranes ruptured, head well down and in second stage  $2\frac{1}{2}$  hours.

Induction - Secondary inertia.

F.H. shows marked drop and then recovery.

Child born in good condition.

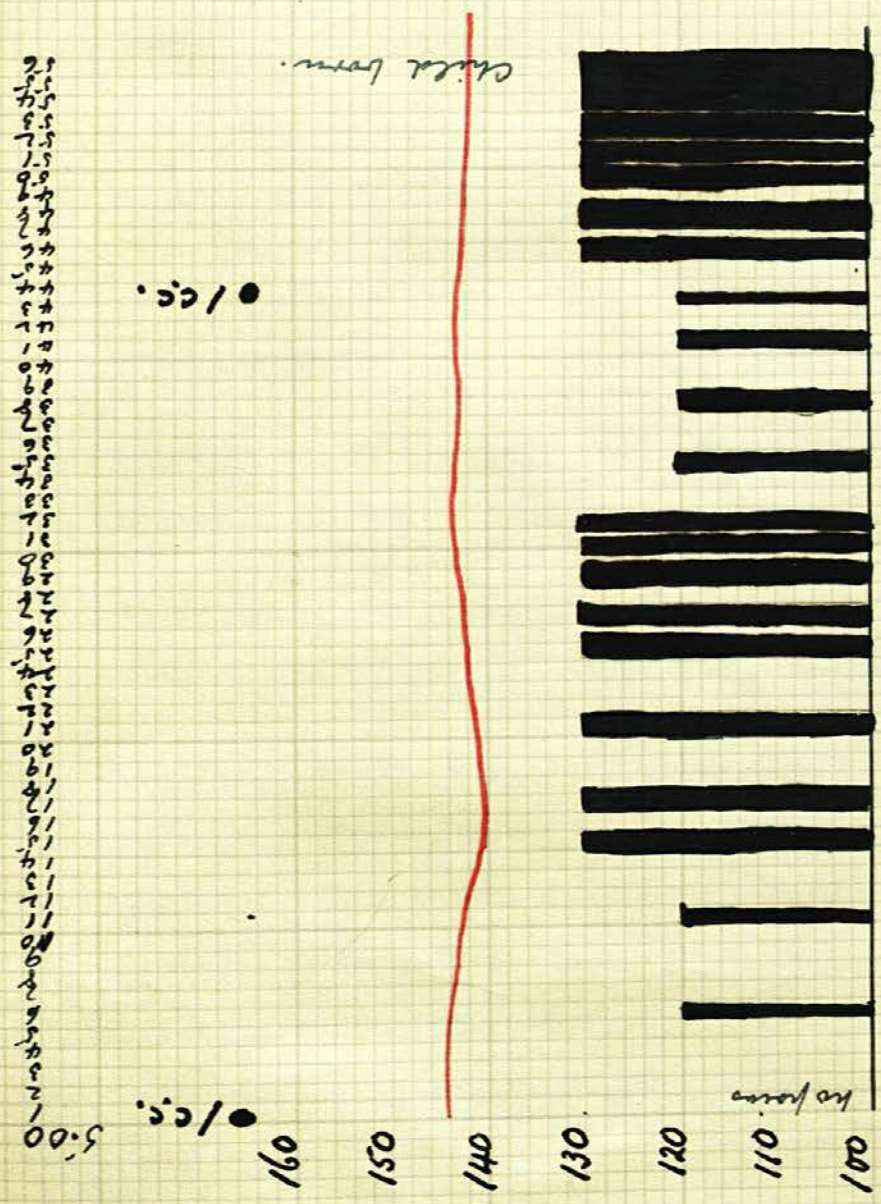
Was premature 8 months and weighed  $3\frac{3}{8}$  lbs.

Died shortly after birth.

Placenta in 30 minutes.

no P.P.H.





See Diagram I for explanation of scheme.

E. F. age 35 VIII para.  
 A case of twins where  
 pains ceased after birth  
 of the first child 40  
 minutes previously.  
 Indication - Inertia.  
 F. H. unaffected.  
 Placenta in 30 minutes  
 to P. P. H.

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